1634

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
(Case No. 142/003/PCT; 03-776)

PATENT

In re Application of:	**Light et al.**	
Serial No.:	**09/582,492**	**Before the Examiner:** **J. Switzer**
Filed:	**March 6, 2002**	**Group Art Unit:** **1634**
For:	**Detection of Human Papilloma Virus in Papanicolaou (Pap) Smears**	

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

TRANSMITTAL LETTER

1. We are transmitting herewith the attached papers for the above-described patent application: Response to Communication and return postcard.

2. GENERAL AUTHORIZATION TO CHARGE OR CREDIT FEES: Please charge any additional fees or credit any overpayment to Deposit Account No. 13-2490.

3. CERTIFICATE OF MAILING UNDER 37 C.F.R. § 1.8: The undersigned hereby certifies that this Transmittal Letter and the papers, as described in paragraph 1, are being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on September 17, 2004.

Respectfully submitted,
McDonnell Boehnen Hulbert & Berghoff

Dated: September 17, 2004

By: _____
Donald L. Zuhn, Ph.D.
Reg. No. 48,710

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P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

RESPONSE TO COMMUNICATION MAILED AUGUST 17, 2004

Responsive to the Communication mailed August 17, 2004, and pursuant to 37 C.F.R. § 1.133, Applicants provide the following remarks regarding the substance of the Interview on July 27, 2004 between Examiner Juliet Switzer, Primary Examiner Jeff Fredman, Huw Jones of Assignee Ventana Medical Systems, Inc., and Applicants' undersigned representative.

At the Interview, Applicants' representative presented two exhibits (see attached) to illustrate that the process of labeling a full-length template by nick translation generates labeled fragments from the full-length template. Applicants' representative contended that by using nick translation, or another suitable labeling technique (such as the PCR amplification or random priming techniques described in the instant specification), to label an HPV genomic template, one of ordinary skill in the art would generate a DNA probe set comprising a plurality of nucleic acid molecules that detectably hybridize to substantially all of the full-length HPV genomic template from which the DNA probe set was generated. In other words, the DNA probe set would comprise a plurality of nucleic acid molecules that substantially "cover" the full-length HPV genomic template. Applicants' representative noted that the range of fragments generated using nick translation would depend upon

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Donald L. Zuhn

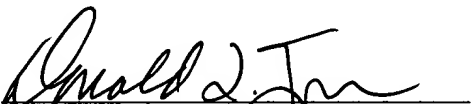
factors such as the quality of the HPV genomic template and the amount of DNAse I added to the labeling reaction mixture.

During the Interview, amendments to claim 1 were discussed which would clarify that the claimed reagents comprise a plurality of genomic HPV DNA probe sets, wherein each probe set comprises a plurality of nucleic acid molecules that detectably hybridize to substantially all of the full-length genomic sequence of a particular HPV type. Applicants submitted an Amendment on August 4, 2004, to incorporate the claim amendments that were discussed during the Interview. Applicants note that no prior art was discussed at the Interview.

Applicants respectfully contend that all conditions of patentability are met in the pending claims as amended. Allowance of the claims is thereby respectfully solicited. If Examiner Switzer believes it to be helpful, she is invited to contact the undersigned representative by telephone at 312-913-0001.

Respectfully submitted,
McDonnell Boehnen Hulbert & Berghoff

Dated: September 17, 2004

By: 
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Chicago, Illinois 60606
312-913-0001

DNA labeling by nick translation

reagents:
DNA for labeling (concentration c > 150 ng/µl)
modified nucleotides: Biotin-16-dUTP, Digoxigenin-11-dUTP, conc. 1nmol/µl (Boehringer Mannheim)
dNTPs (regular nucleotides): dATP, dCTP, dGTP, 0.5 mM each, dTTP 0.1 mM
NT reaction buffer 10x (0.5 M Tris pH 8, 50 mM $MgCl_2$, 0.5mg/ml BSA)
β-ME (beta-mercaptoethanol) 0.1 M
DNase (stock solution 3 mg/ml) 1:2000 diluted in aqua bidest.
Pol: Kornberg DNA-polymerase 5 U/µl (e.g. Boehringer Mannheim)
EDTA (0.5 M, pH 8.0)
SDS (20%)

for one NT reaction 5 µg of DNA is used:

Mix (V total = 50 µl):	1 probe	mix for N probes	
NT (10x)	5 µl	(N+1) * 5 :	
β-ME	5 µl	(N+1) * 5 :	for more than 1 probe
dNTPs	5 µl	(N+1) * 5 :	pipette 19 µl to the
Bio/Dig-dUTP*	2 µl	(N+1) * 2 :	DNA+H_2O
DNase (1:2000)	1 µl	(N+1) * 1 :	
Pol	1 µl	(N+1) * 1 :	
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DNA+H_2O	31 µl		
	=====		
	50 µl		

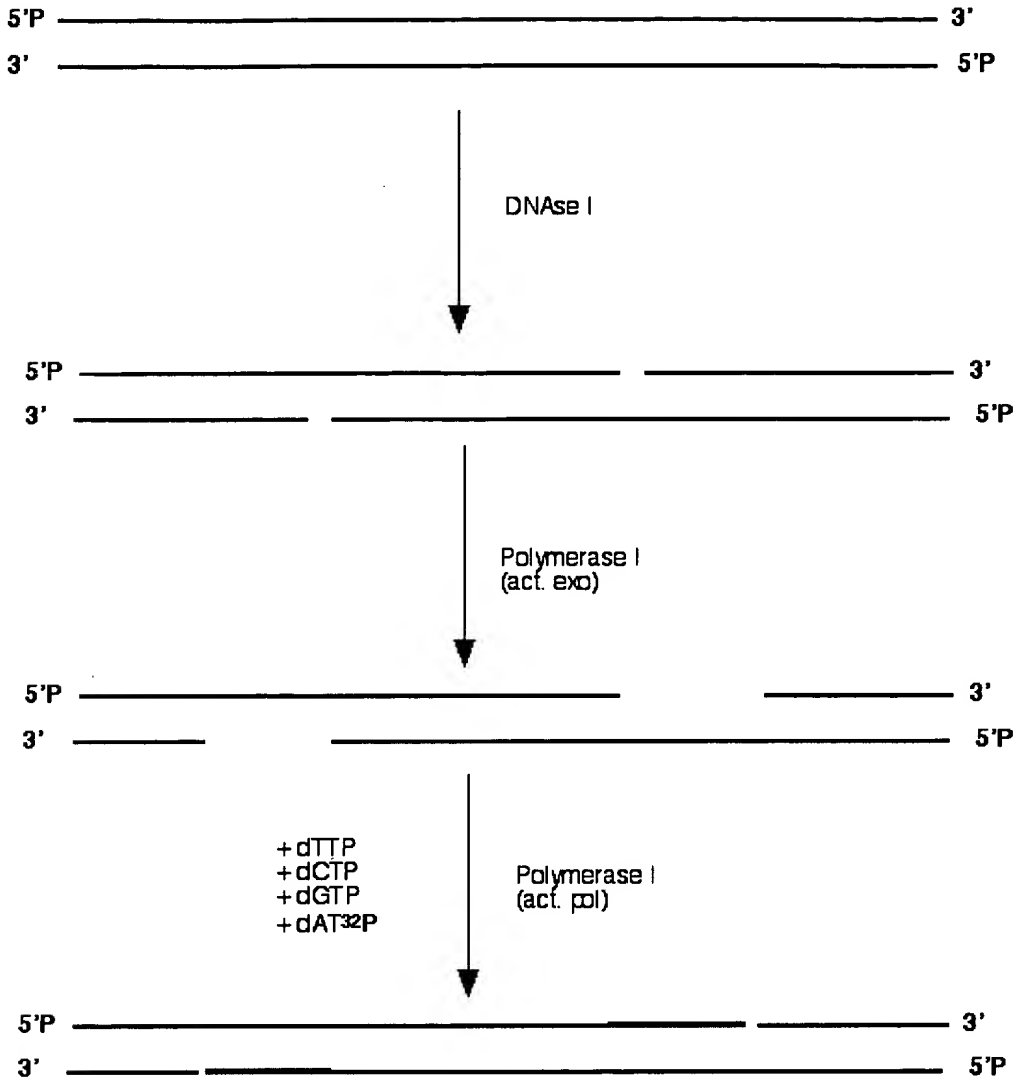
*in the standard protocol Tumor DNA is labeled with Bio-dUTP, Normal DNA is labeled with Dig-dUTP

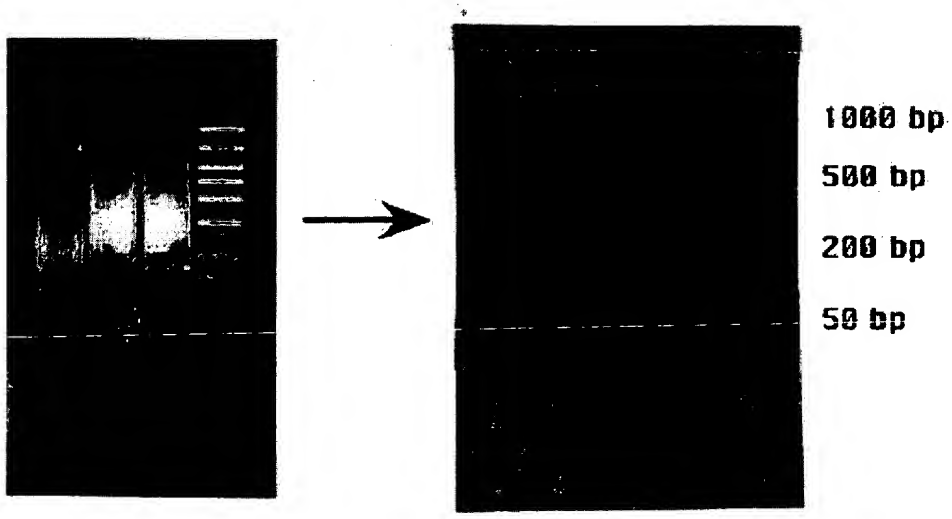
Pipette on ice!

incubation for 2 hrs at 15°C --> put probes on ice --> test 5 µl of the mix in an agarose electrophoresis, optimal length of DNA fragments should be between 100-1000 bp (in the mean time store probes at -20°C)
-->if neccessary incubate longer after addition of new DNAse and Pol
-->add 2.5 µl EDTA (0.5 M, pH 8.0) and 2.5 µl SDS (20%) to stop the reaction, keep the probes at -20°C until hybridization

Optimal fragment length after nick translation

DNA after agarose gel electrophoresis ===> Detection of labeled DNA by a color reaction after transfer to a nylon membrane





CGH